Serial No.:

09/039,927

Filed:

March 16, 1998

List of Claims

18. (currently amended) A method for screening for agents that inhibit the activity of a Kir3.0 channel, the method comprising:

- a) combining at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel;
- b) combining the candidate agent with said Kir3.0 channel under conditions that permit inward K+ current;
- c) determining the induced current, wherein a reduction in said induced current in the presence of said agent as compared to a control is indicative that said agent inhibits the activity of a Kir3.0 channel.

wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12, and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16.

- 19. (canceled)
- 20. (canceled)
- 21. (currently amended) A method for screening for agents that inhibit the activity of a Kir3.0 channel, the method comprising:
- a) providing a functional Kir3.0 channel formed by introducing into an expression host cell a nucleic acid encoding a first mammalian Kir3.0 polypeptide and a nucleic acid encoding a second mammalian Kir3.0 polypeptide under conditions that permit expression of said nucleic acid, wherein said first and second mammalian Kir3.0 polypeptides are different from each other, wherein said mammalian Kir3.0 polypeptides assemble to form a functional Kir3.0 in said expression host cell;
- b) combining a candidate agent with a functional Kir3.0 channel under conditions that permit inward K+ current;
- c) determining the induced current, wherein a decrease in said induced current in the presence of said agent as compared to a control is indicative that said agent inhibits the activity of a Kir3.0 channel,

Serial No.:

09/039,927

Filed:

March 16, 1998

wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12, and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16.

22. (canceled)

- 23. (currently amended) A screening assay for identifying materials which inhibit the activity of a Kir3.0 channel, comprising the steps of:
- (a) introducing nucleic acid encoding a Kir3.0 channel formed from at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides into an expression system and causing the expression system to express said nucleic acid encoding a Kir3.0 channel;
 - (b) contacting the Kir3.0 channel with one or more candidate channel-inhibiting materials;
- (c) selecting candidate material(s) which inhibit said activity relative to a control performed in their absence,

wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides having at least about 50% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12, and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16.

24. (canceled)

- 25. (new) A method for screening for agents that inhibit the activity of a Kir3.0 channel, the method comprising:
- a) combining at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides to form a functional Kir3.0 channel;
- b) combining the candidate agent with said Kir3.0 channel under conditions that permit inward K+ current;
- c) determining the induced current, wherein a reduction in said induced current in the presence of said agent as compared to a control is indicative that said agent inhibits the activity of a Kir3.0 channel,

Serial No.: 09/039,927

Filed: March 16, 1998

wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides encoded by nucleic acids that hybridize under low stringency conditions with a complement of the nucleic acid of SEQ ID NO: 7, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:16.

26. (new) A method for screening for agents that inhibit the activity of a Kir3.0 channel, the method comprising:

- a) providing a functional Kir3.0 channel formed by introducing into an expression host cell a nucleic acid encoding a first mammalian Kir3.0 polypeptide and a nucleic acid encoding a second mammalian Kir3.0 polypeptide under conditions that permit expression of said nucleic acid, wherein said first and second mammalian Kir3.0 polypeptides are different from each other, and wherein said mammalian Kir3.0 polypeptides assemble to form a functional Kir3.0 in said expression host cell;
- b) combining a candidate agent with said functional Kir3.0 channel under conditions that permit inward K+ current; and
- c) determining the induced current, wherein a decrease in said induced current in the presence of said agent as compared to a control is indicative that said agent inhibits the activity of a Kir3.0 channel,

wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides encoded by nucleic acids that hybridize under low stringency conditions with a complement of the nucleic acid of SEQ ID NO: 7, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:16.

- 27. (new) A screening assay for identifying materials which inhibit the activity of a Kir3.0 channel, comprising the steps of:
- (a) introducing nucleic acid encoding a Kir3.0 channel formed from at least two different inward rectifier, G-protein activated, mammalian, potassium Kir3.0 polypeptides into an expression system and causing the expression system to express said nucleic acid encoding a Kir3.0 channel;
 - (b) contacting said Kir3.0 channel with one or more candidate channel-inhibiting materials;
- (c) selecting candidate material(s) which inhibit said activity relative to a control performed in their absence,

Serial No.: 09/039,927

Filed: March 16, 1998

wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides encoded by nucleic acids that hybridize under low stringency conditions with a complement of the nucleic acid of SEQ ID NO: 7, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:16.

28. (new) The method of claim 18, wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides having at least about 75% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 and a Kir3.4

29. (new) The method of claim 21, wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides having at least about 75% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16.

30. (new) The method of claim 23, wherein said Kir3.0 polypeptides are selected from the group consisting of polypeptides having at least about 75% amino acid sequence identity with a Kir3.1 polypeptide encoded by the nucleic acid of SEQ ID NO: 7, a Kir3.2 polypeptide encoded by the nucleic acid of SEQ ID NO:11, a Kir3.3 polypeptide encoded by the nucleic acid of SEQ ID NO:12 and a Kir3.4 polypeptide encoded by the nucleic acid of SEQ ID NO:16.